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Note

Molecular Mechanics Calculations on a New Model Compound Cu(II)–Zn(II)–Superoxide Dismutase

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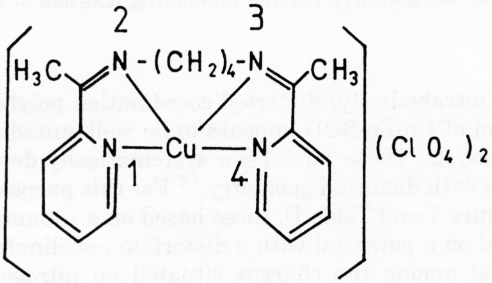
The X-ray structure of a new model compound of Cu(II)-Zn(II)-superoxide dismutase, [*N,N'*-butylenebis(2-acetylpyridineiminato)]copper(II) perchlorate was subjected to molecular mechanics calculations in order to reproduce the shape of the copper(II) coordination polyhedron. Altogether, six force fields were used; three of them yielded good agreement between theory and experiment, the rest gave structures highly distorted from planarity. The results suggest inadequacy of some molecular mechanics models for the simulation of highly distorted structures.

A new model compound of Cu(II)-Zn(II)-superoxide dismutase (Cu-Zn-SOD), [*N,N'*-butylenebis(2-acetylpyridineiminato)]copper(II) diperchlorate, (see Scheme I) has been recently synthesized and studied by the Chinese group.[1] Enzymatic tests revealed its activity to be 10% that of Cu-Zn-SOD and twenty-eight times that of $Na_2[Cu(salicylate)_2]$. The high enzymatic activity is closely related with the structural similarity to the active centre of the native enzyme.[2]



Scheme I

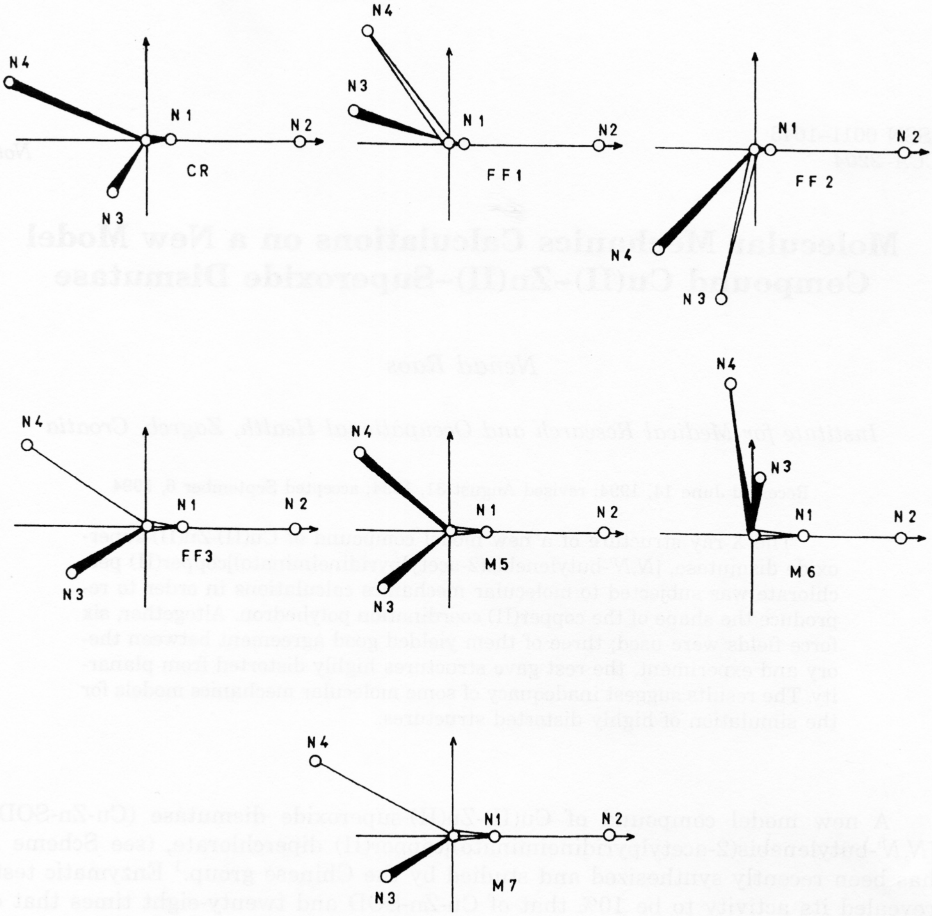


Figure 1. Copper(II) coordination polyhedra of [*N,N'*-butylenebis(2-acetylpyridineiminato)]copper(II) diperchlorate, as obtained by X-ray analysis[1] (CR) and molecular mechanics calculations (FF1, FF2, FF3, M5, M6 and M7). For the numbering notation of nitrogens see Scheme I.

Having a higly (tetrahedrally) distorted coordination polyhedron (Figure 1), the new model compound of Cu-Zn-SOD appears to be well suited for checking our molecular mechanics models. These have been systematically developed for the study of copper(II) chelates with distorted geometry.[3–7] For this purpose, six empirical force fields were used (Figure 1 and Table I), three based on a »dummy« atom model (FF1, FF2, FF3)[3] one based on a potential with a distortion coordinate (M5)[5] and two with a coulombic potential among the charges situated on nitrogens and two charges placed above and below the plane of the chelate rings (M6, M7).[6,7]

As it can be seen from the Figure 1, upon minimization of conformational energy based on three force fields (FF3, M5 and M7), the crystal structure converged to a

TABLE I

Comparison of crystal structure (CR) with the structures obtained by molecular mechanics calculations*

	CR	FF1	FF2	FF3	M5	M6	M7
Cu-N1	1.966	1.967	1.961	1.991	2.001	2.078	2.052
Cu-N2	2.006	1.911	1.968	1.989	2.013	2.086	2.054
Cu-N3	1.96	1.968	2.091	1.988	2.008	2.073	2.054
Cu-N4	1.992	2.045	2.034	1.996	2.003	2.092	2.052
N1-Cu-N2	82.0	86.0	83.2	78.2	76.3	72.6	75.2
N3-Cu-N4	81.7	75.4	67.3	77.6	76.2	74.0	75.5
N2-Cu-N3	102.0	128.4	77.9	119.4	115.6	89.7	116.3
N1-Cu-N4	102.9	72.2	177.4	99.7	105.4	87.2	101.8
N1-Cu-N3	159.3	142.4	71.4	153.6	154.6	151.8	160.5
N2-Cu-N4	156.6	123.3	128.6	144.1	149.3	99.6	152.0
$\varepsilon_{\mathrm{r.m.s.}}(\Delta\Theta)$		22.7	39.8	9.4	7.4	25.3	7.2

* Bond lengths are expressed in Å and valence angles in degrees. The root-mean-square deviation, $\varepsilon_{\mathrm{r.m.s.}}(\Delta\Theta)$, refers to the difference in valence angles between the experimental and the theoretical structures. The parameters for molecular mechanics calculations are reported elsewhere.[11,12] Calculations were performed by means of a program developed by Kj. Rasmussen and co-workers.[13]

configuration with a tetrahedrally distorted square-planar coordination of copper(II). The values of the root-mean-square deviation obtained with these force fields (Table I) were acceptable but less successful than usual (*cf.* the values of 2 to 4° obtained for copper(II) aminoacidates with distorted geometry).[5–9] Unfortunately, force fields FF1, FF2 and M6 yielded pyramidally distorted square-planar structures with a substantially higher r.m.s. deviation.

The reason for this discrepancy is not clear at first. The »bad« force fields FF1 and FF2 belong to the same »dummy« atom model as the »good« one (FF3). The model with a coulombic potential in the first coordination sphere (M6) yielded generally the best results for copper(II) aminoacidates,[10] but it obviously failed in this case.

The common characteristics of force fields FF1 and FF2 are very high values of the parameters for the N-Cu-N (*cis*) valence-angle bending potential (97.784 kcal mol^{-1} rad^{-2}), actually parametrized for cobalt(III) complexes (*cf.* 11.0 kcal mol^{-1} rad^{-2} for FF3). This parametrization obviously led, in the impossibility to obtain a square-planar structure, to the configuration as close to the structure with N-Cu-N (*cis*) = 90° as possible, *i.e.* to the pyramidal arrangement of nitrogen atoms around copper. In the case of force field M6 – as shown previously[6] – there was a very deep pyramidal »false« minimum on the potential energy surface for copper complexes, in which highy distorted initial structure should converge. This problem seems to be solved in the improved coulombic model M7.[7]

The answer why the convergence to »false« minima did not happen in previous calculations on coordination compounds lies possibly in the very high distortion of the coordination polyhedron of the new Cu-Zn-SOD model compound ($\varepsilon_{\mathrm{r.m.s.}}(\Delta\Theta) = 15.4°$ for distortion from planarity, *cf.* 3.0 for 7.0° for aminoacidates).[5] We will try to find the final answer to this assumption by doing molecular mechanics calculations on a series of copper(II) chelates with very distorted structures.

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SAŽETAK

Molekulsko-mehanički proračuni na novom modelnom spoju Cu(II)-Zn(II)-superoksid dismutaze

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Rentgenska struktura novog modelnog spoja Cu(II)-Zn(II)-superoksid-dismutaze, [*N,N'*-butilenbis(2-acetilpiridiniminato)]bakrova(II)perklorata proračunana je molekulsko-mehaničkom metodom u namjeri da bi se reproducirao oblik koordinacijskog poliedra dvovalentnog bakra. Ukupno je iskušano šest polja sila: tri su polučila dobro slaganje između teorije i eksperimenta, dok su ostala dala distordirane izrazito neplanarne stukture. Rezultati upućuju na neprikladnost nekih molekulsko-mehaničkih modela za simulaciju vrlo distordiranih struktura.